Remarks

Claims 1-12 are pending in this application.

Claim Rejections - 35 USC §103

Claims 1-12

The Examiner has rejected these claims as being obvious over Spasic et al. (1995, Conference on Selenium - 1993), 119-130), over Dong et al. (J. Trace Elements in Experimental Medicine 10:163-171 (1997), and further in view of U.S. Patent Application No. 20010044431 to Rodriguez.

The Examiner contends that Spasic et al. teach pretreatment with selenium compound can reduce the toxic effects of doxorubicin. Applicants respectfully disagree. This reference discloses an effect of FERKSEVIT (combination of selenium, vitamin E and C and carotene) on the toxicity of doxorubicin. From these data it is not clear if selenium alone would have any effect on reducing toxicity of doxorubicin. Further, it should be noted that Spasic et al. evaluated the effects of on tissues such as liver, kidney, heart and small intestines (page 121, Materials and Methods). Typically, bone marrow toxicity is the primary dose limiting toxicity of doxorubicin in animals and patients and there is no indication that the markers evaluated by Spasic et al. are predictive of doxorubicin toxicity seen in vivo

Dong et al. describe the protective effect of selenium on the toxicity of 5-FU. It should be noted that toxicity of various anticancer agents is based on different mechanisms as is evidenced by organs being differentially affected by different anticancer agents. Thus, for example, while toxicity associated with cisplatin is often seen as renal toxicity, and with adriamycin as cardiotoxicity, the toxicity associated with irinotecan is generally gastrointestinal toxicity and neutropenia. Accordingly, it is not obvious that reduction of toxicity of one anticancer agent can be extrapolated to others. 5-FU is an anti-metabolite and inhibits thymidylate synthase. The mechanisms of action of doxorubicin and oxaliplatin are quite different. These do not act via the same mechanism as 5-FU. Doxorubicin is a topoisomerase II inhibitor while oxaliplatin is a DNA alkylating agent.

The reference of Rodriguez is directed toward the effect of selenium for inhibiting the conversion of normal epithelial cells to cancer cells (paragraph 0014) by inducing the expression of TGF-β. There is no teaching or suggestion to that selenium can reduce the toxicity of doxorubicin or oxaliplatin.

Therefore, Applicants respectfully submit that these references do not teach or even suggest that toxicity of therapeutically effective doses of doxorubicin or oxaliplatin can be reduced by selenium compounds. Accordingly, withdrawal of this rejection is respectfully requested.

Double Patenting

Applicants herewith file a Terminal Disclaimer with respect to U.S. patent application no. 10/844,800.

Conclusion

Based on the above arguments and amendments, Applicants believe that claims 1-12 are now in a condition for allowance and therefore respectfully request the Examiner to allow these claims.

This application is being filed with a request for one-month extension. A check for $60.00 is enclosed. If any additional fee is due, it may be charged to Deposit Account No. 08-2442.

Respectfully submitted,
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